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Computational Modeling of the Structure-Function Relationship in Human Placental Terminal Villi

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Abstract

Placental oxygen transport takes place at the final branches of the villous tree and is dictated by the relative arrangement of the maternal and fetal circulations. Modeling techniques have failed to accurately assess the structure-function relationship in the terminal villi due to the geometrical complexity. Three-dimensional blood flow and oxygen transport was modeled in four terminal villi reconstructed from confocal image stacks. The blood flow was analyzed along the center lines of capillary segments and the effect of the variability in capillary diameter, tortuosity and branching was investigated. Additionally, a validation study was performed to corroborate the simulation results. The results show how capillary variations impact motion of the fetal blood, and how their bends and dilatations can decelerate the flow by up to 80%. Vortical flow is also demonstrated not to develop in the fetal capillaries. The different geometries are shown to dictate the transport of gases with differences of over 100% in the oxygen flux between samples. Capillary variations are key for efficient oxygen uptake by the fetus; they allow the blood to decelerate where the villous membrane is thinnest allowing for a better oxygenation, but also by reducing the vessel diameter they carry the oxygenated blood away fast. The methodology employed herein could become a platform to simulate complicated *in-vivo* and *in-vitro* scenarios of pregnancy complications.

Keywords: Blood Flow, Oxygen Transport, Terminal Villi, Placenta, Modeling

1. Introduction

The importance of placental blood circulation was already noted by Aristotle On the Generation of Animals, *ca* 340 B.C., due to its role in the transport of respiratory gases from the mother to her fetus. Because of the *in-vivo* ethical limitations and the complicated acquisition and manipulation of the *ex-vivo* organ, placental research has been very challenging. Furthermore, animal models are of limited use due to species differences in structure and biochemistry of the placenta (Battaglia and Meschia, 1986). As a consequence, the functional relationships between the maternal and fetal blood streams, at the level of the terminal villus (microscopic scale), are not well understood.

Maternal blood enters the placenta when it reaches the intervillous space via the uterine arteries, percolates between branches of the villous tree and returns deoxygenated to the maternal circulatory system through the uterine veins. On the other side, fetal blood flows from the umbilical arteries towards the branching trees of the chorionic vasculature, and oxygenated blood returns via the umbilical vein (Figure 1). The feto-placental capillaries are tortuous, have variable diameters and sharp bends (Plitman Mayo et al., 2016), making their architecture unique. The two circulations are brought into proximity in the villous tree, separated by the villous membrane. Placental gas exchange takes place at the terminal villi where vasculo-syncytial membranes form (Gill et al., 2011). These are localised areas where the membrane is thinnest, often as little as 1-2 μm (Burton and Tham, 1992).

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